throughout the specification, including the originally filed claims.

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the subject matter of the invention, and to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Restriction Requirement

In the Response to Restriction Requirement filed on July 10, 2002, Applicants had elected the *species* of SEQ ID NO:6. It is Applicants' understanding that, under 35 U.S.C. §121, an election of a single species for prosecution on the merits is required, to which the claims will be restricted if no generic claim is finally held allowable. Applicants submit that claim 19 is generic. Applicants further understand that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141.

Priority

With respect to Applicant's claim for domestic priority, the Examiner is of the opinion that

> Applicant's claim for domestic priority under 35 U.S.C. 119 (e) is acknowledged. This application claims a priority of Application No. 60/201,261, filed on May 2, 2000. This Application fails to provide the sequences claimed in a printed or computer readable form. Therefore, the priority date granted is August 22,2000, which is a filing date of this application.

Applicants respectfully traverse the Examiner's determination that the instant application is only entitled to an August 22, 2000 priority date. Applicants respectfully submit that, as evidenced by copies of pages 45 and 46 of provisional application serial no. 60/201,261 (submitted herewith as

Appendix B), the provisional application contained the sequences that are being claimed in the instant application. The parts of a *provisional* application that are required to establish a priority date are set forth in 37 C.F.R. § 1.51(c) and M.P.E.P. § 601.01(b). The filing of a Sequence Listing (in a printed or computer readable form) is ***not*** required to establish a priority date. Thus, the disclosure of the claimed sequences in provisional application serial no. 60/201,261 is all that is required to satisfy the requirements of 35 U.S.C. §112 and establish Applicants' right to the domestic priority under 35 U.S.C. §119 (e). In view of all of the foregoing, Applicants submit that they are entitled to the priority date of May 2, 2000 (the filing date of the provisional patent application).

Rejection of Claims 19-22 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 19-22 under 35 U.S.C. §112, first paragraph because, according to the Examiner, "the specification, while being enabling for an isolated peptide comprising an amino acid sequence set forth in SEQ ID NO:6; does not reasonably provide enablement for all mutants or fragments generated from any position located *on* the sequence of SEQ ID NO: 6." In particular, the Examiner is of the opinion that

> [t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Claims 19-22 encompass an isolated peptide comprising an amino acid sequence set forth in SEQ ID NO: 6 and the fragments, mutants and variants thereof (claim 19), a composition comprising the said peptides (claim 20) and a carrier (claim 21), an isolated peptide consisting of the amino acid sequence of SEQ ID NO: 6 (claim 22). The specification, however, only discloses cursory conclusions (see page 13-15), without data to support the findings, which state that the molecules that down-regulate interaction of NEMO with the IKK complex is part of the invention. The specification further indicates at page 14 that binding agents specific to NEMO, capable of blocking interaction of NEMO at the nemo-binding domain (NBD) on IKKjS. Exemplary IKK/? inhibitors include competitive inhibitors of NEMO binding at the NBD, for example, the peptide -set forth in SEQ ID NO: 2 and conservative substitution thereof, which has no significant effect on NEMO binding at NBD (Table 1). There are no indicia that the present application enables the full scope in view of the peptides of SEQ ID NO: 1 and a mutant thereof as discussed in the following stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is encompassed.

Applicants respectfully traverse the foregoing rejection on the grounds that the teachings in Applicants' specification are sufficient to enable one of skill in the art to make and use the claimed invention using only routine experimentation. However, in the interest of expediting prosecution and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended the claims, thereby rendering the foregoing rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 19-22 Under 35 U.S.C. §102(a)

The Examiner has rejected claims 19-22 under 35 U.S.C. §102(a) as anticipated by Bower *et al.* (WO 99/31255). The Examiner relies on Bower *et al.* for teaching "an EGIII-like cellulase of Gliocladium roseum, which has 92.5% sequence identity to SEQ ID NO: 6 (see sequence alignment result, A_Geneseq_032802 database, Accession NO: AAY06332, September 6,1999)." The Examiner is of the opinion that

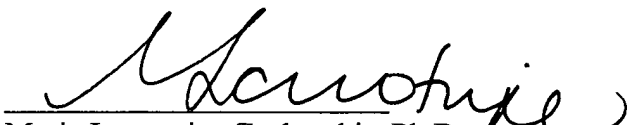
> [t]his reads on claims 19,20 and 21, which has any size of fragment, any number of substitutions both singly and/or in any combination (claim 19,22). See the sequence alignment attached to the Bower et al. reference. As to claims 20 and 21, the Bower et al. reference discloses a composition comprising the celluliise (page 21, lines 6-8) that would have been the composition that contains the peptide of claim 19.

Applicants respectfully traverse the aforementioned rejection on the grounds that Bower *et al.* fail to teach or suggest each and every element of the claimed invention. However, in the interest of expediting prosecution and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended the claims, thereby rendering the foregoing rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



Maria Laccotripe Zacharakis, Ph.D.
Attorney for Applicants
Limited Recognition Under 37 C.F.R. § 10.9(b)

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400

Dated: February 24, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend claim 19, 20 and 22 as follows:

19. **(Amended)** An ~~isolated peptide selected from the group consisting of:~~

~~(a) an~~ isolated peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17, 18 and 19~~;~~

~~(b) an isolated peptide comprising a fragment of at least three amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19;~~

~~(c) an isolated peptide comprising conservative amino acid substitutions of the amino acid sequences selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19; and~~

~~(d) naturally occurring amino acid sequence variants of amino acid sequences selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19~~.

20. **(Amended)** A composition comprising the peptide of claim ~~15 or~~ 19 or 22.

22. **(Amended)** An isolated peptide consisting of ~~the~~ an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

Please add new claims 24-27 as follows:

24. A fusion peptide comprising the peptide of claim 19 or 22.

25. A fusion peptide comprising the peptide of claim 19 or 22 and at least one membrane translocation domain.

26. The fusion peptide of claim 25, wherein said membrane translocation domain comprises the third helix of the *antennapedia* homeodomain.

27. The fusion peptide of claim 25, wherein said membrane translocation domain comprises the HIV-1 Tat protein.

APPENDIX A

19. An isolated peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17, 18 and 19.

20. A composition comprising the peptide of claim 19 or 22.

21. The composition of claim 20 further comprising a carrier.

22. An isolated peptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

24. A fusion peptide comprising the peptide of claim 19 or 22.

25. A fusion peptide comprising the peptide of claim 19 or 22 and at least one membrane translocation domain.

26. The fusion peptide of claim 25, wherein said membrane translocation domain comprises the third helix of the *antennapedia* homeodomain.

27. The fusion peptide of claim 25, wherein said membrane translocation domain comprises the HIV-1 Tat protein.

Table 1. Characterized NBD mutant peptides and their ability to bind to NEMO.

NBD Mutant Peptide†	Binds to NEMO	SEQ ID NO:
LDWSWL	yes	2
LDASAL	no	3
ADWSWL	yes	4
LDWSWA	yes	5
ADWSWA	yes	6
LAWSWL	no	7
LEWSWL		8
LNWSWL		9
LDASWL	no	10
LDFSWL	yes	11
LDYSWL	yes	12
LDWSAL	no	13
LDWSFL	no	14
LDWSYL	no	15
LDWAWL	yes	16
LDWEWL	yes	17

† The substituted amino acid residue is indicated by bold face.

Example 5 - Agents which interact with NBD to block NEMO binding

The relatively small size of the NBD makes it an attractive target for the development of compounds aimed at disrupting the core IKK complex. The relevance of this approach was investigated by designing cell-permeable peptides spanning the IKKβ

NBD and determining their ability to dissociate the IKKβ-NEMO interaction.

The sequences of the two NBD peptides used in this study were [DRQIKIWFQNRRMKWKK]TALDWSWLQTE (wild-type) (SEQ ID NO: 18) and [DRQIKIWFQNRRMKWKK]TALDASALQTE (mutant) (SEQ ID NO: 19). The *antennapedia* homeodomain sequence (Derossi *et al.*, J. Biol. Chem. (1994) 269, 10444-10450; U.S. Patent No. 5,888,762; U.S. Patent No. 6,015,787) is bracketed and the positions of the W→A mutations are underlined. Both peptides were dissolved in DMSO to a stock concentration of 20 mM. For all experiments DMSO alone controls were no different from no peptide controls.

The wild-type NBD peptide consisted of the region from T735 to E745 of IKKβ fused with a sequence derived from the third helix of the antennapedia homeodomain that has been shown to mediate membrane translocation (Derossi *et al.*, J. Biol. Chem. (1994) 269, 10444-10450). The mutant peptide was identical except that the tryptophan residues (W739 and W741) in the NBD were mutated to alanine. Figure 5A shows that the NBD (WT) but not the mutant peptide dose-dependently inhibited *in vitro* pull-down of [^{35}S]-labeled IKKβ by GST-NEMO and [^{35}S]-labeled NEMO by GST-IKKβ-(644-756). To test the ability of the NBD peptides to enter cells and inhibit the IKKβ-NEMO interaction, HeLa cells were incubated with the peptides for different time periods and immunoprecipitated the IKK complex using anti-NEMO. In agreement with the *in vitro* data (Figure 5A), wild-type but not mutant NBD peptide disrupted the formation of the endogenous IKK complex (Figure 5B).

Example 6 - Agents which block NEMO function

The effects of the NBD peptides on signal-induced activation of NF-κB were investigated next. After transfecting HeLa cells with the pBIIX-luciferase reporter, cells were preincubated with wild-type or mutant peptides, treated with TNFα and NF-κB activation measured by the luciferase reporter assay. As shown in Figure 5C (left panel),